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EFFICACY OF THE QDENGA VACCINE IN THE PREVENTION OF DENGUE: AN INTEGRATIVE REVIEW OF CLINICAL EVIDENCE

EFICÁCIA DA VACINA QDENGA NA PREVENÇÃO DA DENGUE: REVISÃO INTEGRATIVA DAS EVIDENCIAS CLÍNICAS

EFICACIA DE LA VACUNA QDENGA EN LA PREVENCIÓN DEL DENGUE: UNA REVISIÓN INTEGRADORA DE LA EVIDENCIA CLÍNICA

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ABSTRACT

Dengue is one of the most impactful arboviral diseases worldwide, characterized by increasing incidence and persistent challenges in epidemiological control. The Qdenga® (TAK-003) vaccine, developed by Takeda Pharmaceuticals, has emerged as a promising

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preventive alternative with the potential to broaden population protection against the four dengue virus serotypes. This study aimed to critically analyze the scientific evidence available on the clinical efficacy of the Qdenga® vaccine in dengue prevention through an integrative literature review. Data collection was performed in the PubMed, SciELO, LILACS, and Google Scholar databases, including publications from 2017 to 2025 in Portuguese, English, and Spanish. A total of 20 studies were selected, comprising clinical trials, systematic reviews, and epidemiological modeling studies. The results indicate an overall efficacy ranging from 70% to 84%, with a significant reduction in hospitalizations and a low incidence of severe adverse events. The vaccine showed higher effectiveness among previously exposed populations, maintaining a balanced immunogenic profile and adequate safety. It is concluded that Qdenga® (TAK-003) is a relevant and promising tool for global dengue control, and its implementation should be accompanied by continuous epidemiological surveillance and real-world effectiveness studies to consolidate its impact on public health.

Keywords: Clinical Efficacy. Dengue. Integrative Review. Qdenga Vaccine. TAK-003.

RESUMO

A dengue configura-se como uma das arboviroses de maior impacto global, caracterizada por incidência crescente e desafios contínuos no controle epidemiológico. A vacina Qdenga® (TAK-003), desenvolvida pela Takeda Pharmaceuticals, surge como uma alternativa preventiva promissora, com potencial de ampliar a proteção populacional contra os quatro sorotipos do vírus. Este estudo teve como objetivo analisar criticamente as evidências científicas disponíveis sobre a eficácia clínica da Qdenga® na prevenção da dengue, por meio de uma revisão integrativa da literatura. A busca foi realizada nas bases PubMed, SciELO, LILACS e Google Scholar, abrangendo publicações entre 2017 e 2025, nos idiomas português, inglês e espanhol. Foram selecionados 20 estudos, incluindo ensaios clínicos, revisões sistemáticas e modelagens epidemiológicas. Os resultados indicam eficácia global entre 70% e 84%, com redução significativa nas hospitalizações e baixo índice de eventos adversos graves. A vacina demonstrou maior efetividade em populações previamente expostas ao vírus, mantendo perfil imunogênico equilibrado e segurança adequada. Conclui-se que a Qdenga® (TAK-003) constitui uma ferramenta relevante e promissora para o controle global da dengue, cuja implementação deve ser acompanhada por vigilância epidemiológica contínua e estudos de efetividade em condições reais, de modo a consolidar seu impacto em saúde pública.

Palavras-chave: Dengue. Eficácia Clínica. Qdenga. Revisão Integrativa. TAK-003.

RESUMEN

El dengue es una de las enfermedades arbovirales con mayor impacto a nivel mundial, caracterizada por una incidencia creciente y desafíos constantes en su control epidemiológico. La vacuna Qdenga® (TAK-003), desarrollada por Takeda Pharmaceuticals, se presenta como una alternativa preventiva prometedora, con el potencial de ampliar la protección de la población contra los cuatro serotipos del virus. Este estudio tuvo como objetivo analizar críticamente la evidencia científica disponible sobre la eficacia clínica de Qdenga® en la prevención del dengue mediante una revisión bibliográfica integrativa. La búsqueda se realizó en las bases de datos PubMed, SciELO, LILACS y Google Scholar, abarcando publicaciones entre 2017 y 2025, en portugués, inglés y español. Se seleccionaron veinte estudios, incluyendo ensayos clínicos, revisiones sistemáticas y modelos epidemiológicos. Los resultados indican una eficacia general de entre el 70 % y el 84 %, con una reducción significativa de las hospitalizaciones y una baja tasa de eventos

adversos graves. La vacuna demostró mayor efectividad en poblaciones previamente expuestas al virus, manteniendo un perfil inmunogénico equilibrado y una seguridad adecuada. Se concluye que Qdenga® (TAK-003) constituye una herramienta relevante y prometedora para el control mundial del dengue, cuya implementación debe ir acompañada de vigilancia epidemiológica continua y estudios de efectividad en condiciones reales, con el fin de consolidar su impacto en la salud pública.

Palabras clave: Dengue. Eficacia Clínica. Qdenga. Revisión Integrativa. TAK-003.

1 INTRODUCTION

Dengue is currently one of the **most impactful arboviruses globally**, with increasing incidence in more than 100 countries and estimates that exceed **390 million annual infections** (LEE; LONG; POH, 2024). Transmitted mainly by the **Aedes aegypti *mosquito***, the disease manifests clinically from mild to severe forms, such as **hemorrhagic dengue** and **dengue shock syndrome**, which can progress to death (ZEYAULLAH et al., 2022). In recent decades, factors such as **accelerated urbanization**, **climate change,** and **intense population mobility** have contributed to the geographic expansion of the virus, making **isolated vector control insufficient** to contain its spread (SIRIWARDANA; GUNATHILAKA, 2025). Given this scenario, **vaccination** emerges as an **essential strategy for collective prevention**, complementary to **epidemiological surveillance** and **environmental control** measures.

The development of an effective vaccine against dengue, however, has proven to be a **complex scientific challenge**, due to the **existence of four distinct serotypes of the virus** (DENV-1 to DENV-4) and the occurrence of the phenomenon known as **antibody-dependent potentiation (ADE),** which can aggravate the infection in previously seronegative individuals (NHS; THAM, 2025). The first licensed vaccine, **Dengvaxia® (CYD-TDV),** showed **limited efficacy** and **risks of severe disease** in people without prior infection, which restricted its large-scale application (LEE; LONG; POH, 2024). In this context, the **Qdenga® vaccine (TAK-003),** developed by **Takeda Pharmaceuticals**, has emerged as a **second-generation alternative**, as it is a **live attenuated tetravalent vaccine** capable of inducing **a balanced immune response** against the four viral serotypes (ANGELIN et al., 2023).

Clinical evidence from **phase 3 trials** indicates that **Qdenga has** an overall efficacy of between 70% and 84% **against** cases of virologically confirmed dengue**, in addition to**® promoting a **significant reduction in hospitalizations** for severe forms of the disease (PATEL et al., 2023; WILDER-SMITH; CHERIAN, 2025). Studies conducted in populations of **endemic countries**, such as **India, Thailand, and the Philippines**, have shown that the vaccine maintains a **favorable safety profile** and **long-lasting immune response**, even in scenarios of high viral circulation (SAH; AHSAN, 2025; DANIELS; FERGUSON; DORIGATTI, 2024). However, **there was reduced efficacy in seronegative individuals**, particularly against **the DENV-3 and DENV-4** serotypes, which reinforces the need for **continuous immunological monitoring** and **long-term evaluations** (LEE; LONG; POH, 2024).

From a **public health perspective**, the introduction of Qdenga® represents a **milestone in dengue control**. Mathematical models estimate that vaccination of **children in regions with seroprevalence above 60%** can **reduce the number of hospitalizations for dengue by up to 22%** over a period of ten years, evidencing a **positive impact on the burden of disease and care costs** (DANIELS; FERGUSON; DORIGATTI, 2024). The **approval of the vaccine by the European Medicines Agency (EMA)** in 2022 and the **subsequent recommendations of the World Health Organization (WHO)** reinforce its potential for application in **national immunization programs** in areas of high transmission, without the need for prior serological screening (WILDER-SMITH; CHERIAN, 2025). However, **countries with low endemicity** still assess the **risk-benefit ratio** of universal vaccination (ÉPERON et al., 2024).

In view of the advancement of research and the recent **incorporation of Qdenga® into immunization policies**, it is pertinent to gather and critically analyze the **available scientific evidence on its clinical efficacy**. Thus, this integrative review aims to **systematize and synthesize the findings published between 2017 and 2025** regarding **the efficacy of the Qdenga® vaccine (TAK-003)** in the prevention of dengue, contributing to the **improvement of immunization practices** and to the **technical-scientific basis of public health decisions**.

2 METHODOLOGY

2.1 TYPE OF STUDY

It is an **integrative literature review**, conducted according to the methodology proposed by **Whittemore and Knafl (2005),** which makes it possible to integrate empirical and theoretical research results, offering a comprehensive and critical understanding of a given phenomenon. This approach was chosen because it allows the **systematic gathering, evaluation and synthesis of multiple scientific evidences** about the efficacy of the **Qdenga® vaccine (TAK-003)** in the prevention of dengue. The steps followed the recommendations of **Souza, Silva and Carvalho (2010),** which include: identification of the problem, formulation of the guiding question, data collection, evaluation of the included studies, analysis and synthesis of the results.

2.2 GUIDING QUESTION

The research question was elaborated based on the **PICO** (Population, Intervention, Comparison and Outcome) model, adapted for integrative reviews, and defined as follows:

"What is the clinical efficacy of the Qdenga vaccine (TAK-003) in preventing dengue in exposed populations, as per evidence published in the last eight years (2017–2025)?"

With this, the study sought to gather, analyze, and synthesize the available evidence on **efficacy, immunogenicity, and clinical safety** of the Qdenga® vaccine in different age groups and epidemiological contexts.

2.3 DATABASES AND SOURCES OF INFORMATION

Data collection was carried out between **September and November 2025**, in the following internationally recognized databases:

- **PubMed** (U.S. National Library of Medicine);
- **SciELO** (Scientific Electronic Library Online);
- **LILACS** (Latin American and Caribbean Literature on Health Sciences);
- **Google Scholar**, used as a complementary source for grey literature (WHO and EMA reports and technical documents).

The choice of these databases is justified by their **wide coverage of biomedical journals** and their ability to include **international and regional publications** relevant to the epidemiological context of dengue.

2.4 SEARCH STRATEGIES

The bibliographic search was conducted in a **systematic and standardized** way, using **controlled descriptors** of the Medical Subject Headings (MeSH) **and** Health Sciences Descriptors (DeCS) **vocabularies**, in addition **to free keywords** related to the theme. The terms were combined using the **Boolean operators AND and OR** to increase the accuracy and sensitivity of the search.

The survey covered the period from **January 2017 to November 2025**, and considered publications in **Portuguese, English and Spanish**, without geographical restriction. The strategies were adapted according to the specificities of each database, as described below:

2.4.1 PubMed (National Library of Medicine, USA)

The search was performed using the MeSH descriptors and free terms combined as follows: ("Dengue Vaccines"[MeSH]) AND ("TAK-003" OR "Qdenga" OR "Takeda dengue vaccine") AND ("efficacy" OR "effectiveness" OR "clinical trial" OR "immunogenicity").

Filters applied: articles published between 2017 and 2025, studies in humans and Portuguese, English, and Spanish languages. This combination sought to cover clinical trials, systematic reviews, and observational studies on the efficacy, effectiveness, and immunogenicity of the Qdenga® vaccine.

2.4.2 SciELO (Scientific Electronic Library Online)

In the SciELO database, DeCS descriptors and free terms in Portuguese and Spanish were used, combined as follows: (vaccine OR "dengue vaccine" OR "TAK-003" OR "Qdenga") AND (efficacy OR effectiveness OR immunogenicity OR safety) AND (2017-2025).

Filters applied: original articles and reviews, published in Portuguese, English or Spanish. This strategy aimed to identify Latin American publications, especially Brazilian ones, that addressed clinical and public health aspects related to the Qdenga® vaccine.

2.4.3 LILACS (Latin American and Caribbean Literature on Health Sciences)

Controlled descriptors from DeCS were used, combined with free terms, as follows: (dengue AND vaccine* AND (TAK-003 OR Qdenga)) AND (efficacy OR immunogenicity OR safety).

Filters applied: publications between 2017 and 2025, studies with human beings and Portuguese, English and Spanish languages. This strategy aimed to identify relevant regional articles, technical reports, and reviews on the clinical and epidemiological use of Qdenga® in Latin America.

2.4.4 Google Scholar (grey literature and technical papers)

To complement the search, the following expression was used: ("TAK-003" OR "Qdenga") AND "dengue vaccine" AND (efficacy OR effectiveness OR safety) 2017..2025.

This stage aimed to locate **narrative reviews, WHO and EMA reports**, as well as **open access articles** not indexed in traditional databases, ensuring greater coverage in data collection.

All results were exported to **Microsoft Excel® 365** spreadsheets, in which duplicates were eliminated and the essential information of each article (authors, year, country, journal, type of study, objectives, and main results) was recorded. Subsequently, the titles, abstracts and full texts were read, applying the previously defined inclusion and exclusion criteria.

2.5 INCLUSION AND EXCLUSION CRITERIA

2.5.1 Inclusion Criteria:

- Publications between January 2017 and November 2025;
- Original articles, systematic reviews, narrative reviews, modeling studies, and clinical trials;
- Studies published in Portuguese, English or Spanish;
- Research addressing **the efficacy, immunogenicity, or safety** of the Qdenga® vaccine (TAK-003);
- Studies with **human populations** (children, adolescents and adults).

2.5.2 Exclusion Criteria:

- Studies in animal models or in vitro;
- Studies that did not directly address the Qdenga® vaccine;
- Isolated case reports, editorials and letters to the editor;
- Duplicate articles between databases;
- Studies without clinical data relevant to the guiding question.

2.6 SELECTION AND SCREENING OF STUDIES

The selection of studies occurred in **three sequential stages**:

1. **Reading of titles and abstracts**, excluding articles outside the thematic scope;
2. **Complete reading** of eligible studies to verify adherence to inclusion criteria;
3. **Final analysis**, with extraction of essential data (authors, year, country, objectives, type of study, results and conclusions).

The screening process was conducted by **two independent reviewers**, and disagreements were resolved by consensus, ensuring the reliability and validity of the selection process.

2.7 SYNTHESIS AND ANALYSIS OF DATA

The included articles were submitted to **descriptive and interpretative analysis**, and were organized according to thematic similarity and level of evidence. The information extracted was grouped into three main axes:

1. **Clinical efficacy and immunogenicity of Qdenga®;**
2. **Safety and adverse event profile;**
3. **Impact and applicability in public health.**

The synthesis was elaborated in a narrative way, highlighting **convergences, divergences, and knowledge gaps** among the reviewed studies.

2.8 STUDY SELECTION PROCESS (NARRATIVE ADAPTATION OF THE PRISMA 2020 MODEL)

The study selection process followed the steps recommended by **the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020),** adapted to the context of the integrative review. Initially, **248 records were identified** in the **PubMed, SciELO, LILACS, and Google Scholar databases**. After **removing 50 duplicates**, **198 unique studies remained** for initial screening.

In the first stage, the **titles and abstracts were read**, which resulted in the exclusion of **142 articles** because they did not meet the thematic scope or had a different focus on the clinical efficacy of the Qdenga® vaccine. Then, **56 articles** were evaluated in full to verify the eligibility criteria. Of these, **36 were excluded** because they did not present relevant clinical data, did not refer directly to the TAK-003 vaccine, or dealt with non-human experimental models.

At the end of the process, **20 studies** met all the inclusion criteria and were considered suitable to compose the **final body of the integrative review**, serving as a basis for the analysis and synthesis of the results presented in this study.

This procedure ensured **transparency, traceability, and reproducibility** in the selection of articles, as recommended by the principles of PRISMA, reinforcing the methodological reliability of the review.

2.9 ETHICAL ASPECTS

As this is an integrative review based on secondary data in the public domain, **there was no need to submit it to the Research Ethics Committee**, as established by **Resolution No. 510/2016** of the **National Health Council (Brazil).**

3 RESULT AND DISCUSSION

We included **20 articles published between 2017 and 2025**, covering **clinical trials, systematic reviews, epidemiological modeling, and public policy analyses**. Most of the studies were conducted in **endemic countries in Asia and Latin America**, especially **India, Thailand, Brazil, and the Philippines**, and published in high-impact journals such as *Vaccine*, *Travel Medicine and Infectious Disease,* and *Human Vaccines & Immunotherapeutics*. The body of evidence indicates that the **Qdenga® vaccine (TAK-003)** has **an overall efficacy of between 70% and 84%** against virologically confirmed dengue, in addition to a **favorable safety profile in different age groups** (ANGELIN et al., 2023; LEE; LONG; POH, 2024; WILDER-SMITH; CHERIAN, 2025).

Phase 3 clinical trials conducted by **Takeda Pharmaceuticals** demonstrated **robust and sustained immune response** after two doses administered three months apart (PATEL et al., 2023). **Immunogenicity** was observed in both individuals previously exposed to the virus and in seronegative individuals, although efficacy was lower among the latter — especially against the **DENV-3 and DENV-4 serotypes** (LEE; LONG; POH, 2024). This finding is consistent with the reviews by **Siriwardana and Gunathilaka (2025),** which reinforce the need for immune monitoring in populations without prior exposure. On the other hand, in areas of **high endemicity**, such as India and Southeast Asia, the results point to **high protection against hospitalizations and severe forms of the disease**, reaching **up to 84% efficacy** in preventing severe cases (SAH; AHSAN, 2025; DANIELS; FERGUSON; DORIGATTI, 2024).

From a safety **point of view**, the reviewed studies indicate that Qdenga has a® **low rate of serious adverse events**, with the most reported being **local pain, mild fever, and self-limited headache** (ANGELIN et al., 2023; PATEL et al., 2023). No trials reported a significant increase in the risk of disease aggravated by **antibody-dependent** *enhancement (ADE*), although **Tan and Tham (2025)** recommend post-marketing follow-up for long-term safety monitoring. These results differ positively from those observed with **Dengvaxia®**, which presented an increased risk in seronegative individuals (LEE; LONG; POH, 2024).

Regarding **population effectiveness**, **mathematical modeling** studies carried out by **Daniels, Ferguson, and Dorigatti (2024)** estimated that, in regions with **seroprevalence greater than 60%,** childhood vaccination with Qdenga® can reduce the number of dengue hospitalizations by **10% to 22%** in ten years, in addition to reducing hospitalization and mortality costs. Similar results were observed in large-scale implementation analyses **in India**, which demonstrated **positive public acceptance and relevant initial health impact** (SAH; AHSAN, 2025). In a convergent way, **Wilder-Smith and Cherian (2025)** highlight that the incorporation of the vaccine into national immunization programs can be an **effective strategy to reduce the global burden of dengue**, especially in urban centers with high population density.

Regarding **applicability and challenges**, authors such as **Éperon et al. (2024)** and **Fletcher et al. (2025)** emphasize the need for **prior serological screening** in contexts of low endemicity, since the net benefit of vaccination may be lower among seronegative individuals. Even so, both the **World Health Organization (WHO)** and the **European Medicines Agency (EMA)** recommend the use of Qdenga® in **populations over four years of age** living in regions of **continuous transmission**, without the requirement of prior testing (WILDER-SMITH; CHERIAN, 2025). In addition, recent literature reinforces that the **balanced immunogenic profile** and **thermal stability of the vaccine** favor its application in tropical countries, where storage and logistics represent relevant challenges (ANGELIN et al., 2023; HAQUE et al., 2024).

Despite the advances, **significant gaps** still persist. Among the main limitations observed are the **scarcity of clinical data in the elderly over 60 years of age**, the **variation of the immune response** according to the **predominant viral serotype,** and the **absence of prolonged follow-up** in tropical settings (GIANG; TAYLOR-ROBINSON, 2025). In addition, the **methodological heterogeneity between clinical trials** makes direct comparisons of efficacy difficult, as pointed out by **Agustina and Alamanda (2025).** Even so, the body of evidence converges to the understanding that Qdenga represents a milestone in the immune control of dengue, with the potential for significant epidemiological impact in the® medium term.

Thus, the findings of this integrative review show that the **Qdenga® vaccine (TAK-003)** has **consistent clinical efficacy, high immunogenicity, and a satisfactory safety profile**, making it the **most promising alternative currently available** for the global control of dengue. It is recommended that their incorporation into national immunization programs in

endemic countries be accompanied by **active epidemiological surveillance** and **effectiveness studies under real conditions**, with a view to consolidating and expanding the positive impact observed in clinical trials and population modeling.

4 CONCLUSION

The results of this integrative review allow us to conclude that the **Qdenga® vaccine (TAK-003)** constitutes a **significant advance in dengue prevention**, presenting **consistent clinical efficacy**, **high immunogenicity,** and **a favorable safety profile** in different age groups. The evidence analyzed demonstrates **global efficacy between 70% and 84%** in the prevention of virologically confirmed dengue, in addition **to expressive protection against severe forms and hospitalizations** in regions of high endemicity.

The set of studies evaluated indicates that **Qdenga®** is a **safe and well-tolerated** vaccine, with predominantly **mild and self-limiting adverse events**, and **low risk of antibody-dependent potentiation (ADE),** one of the main challenges faced by previous vaccines, such as **Dengvaxia®**. These results reinforce the **potential of Qdenga as a® viable alternative for large-scale use**, especially in **tropical and subtropical countries**, where dengue represents a serious public health problem and an overload for primary care and hospital systems.

From an epidemiological and population **point of view**, the introduction of Qdenga® in national immunization programs has the potential to **significantly reduce morbidity and mortality and hospital costs associated with the disease**, as indicated by the reviewed modeling studies. However, **vaccine efficacy may vary** according to the **predominant viral serotype**, **previous serological status,** and **geographic factors**, which reinforces the importance of **post-marketing surveillance** and **continuous immune monitoring** to ensure effectiveness in different epidemiological contexts.

Despite the advances achieved, **relevant gaps persist** related to the **immune response in the elderly**, the **durability of long-term protection,** and effectiveness **in different endemic populations and regions**. Thus, it is essential to carry out **new multicenter and longitudinal studies**, as well as **comparative research** between Qdenga® and other candidate vaccines, with the aim of expanding the understanding of its relative efficacy and improving immunization strategies against dengue.

In summary, **Qdenga® (TAK-003)** stands out as the **most promising vaccine currently available** for **the global control of dengue**, bringing together **safety, efficacy**

and operational applicability. Its incorporation into national immunization programs should be accompanied by **integrated public policies for vaccination and epidemiological surveillance**, ensuring the **rational, safe, and sustainable use** of this important preventive tool in **reducing the global burden of dengue** and promoting **public health**.

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